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Laboratory Note No. 89-77

Plasma Dextran Concentrations in Trauma
Patients Administered HSD.

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and Perry, J. Holcroft

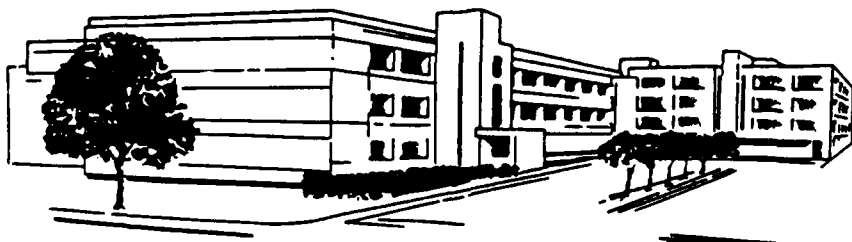
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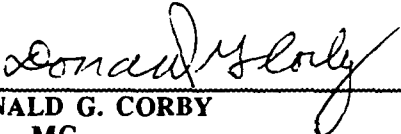
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ABSTRACT

To determine the plasma concentrations of dextran, sodium and potassium, blood samples were obtained from 13 trauma patients treated with hypertonic saline/dextran (HSD). The dose of HSD was 250 ml or 3.6 ± 0.2 ml/kg. Blood samples were taken 27 ± 5 min after the administration of HSD. Plasma levels of sodium were increased (155 ± 1 mEq/l), while potassium concentrations (4.0 ± 0.5 mEq/l) were within normal range. Plasma dextran concentrations (244 ± 27 mg/dl) were significantly less than expected, thereby suggesting either a rapid rate of clearance, association with TCA-precipitable materials, or a larger volume of distribution. These data will provide the basis for future in vitro and in vivo studies as to the efficacy of HSD, and indicate that HSD administration does not result in dangerous alterations in serum electrolyte or dextran concentrations.

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Plasma dextran concentrations in trauma patients administered hypertonic saline/dextran -- Wade et al.

INTRODUCTION

A hypertonic/oncotic solution has recently been introduced for the resuscitation of trauma patients hypotensive due to hemorrhage (1-3). This solution consists of 7.5% NaCl in 6% Dextran-70 and is known as HSD. Concern has been raised as to the degree of hypernatremia and hypokalemia induced by the administration of HSD (1,4,5), as well as possible adverse effects of dextran administration (6-8). The present study investigates the levels of sodium, potassium and dextran in trauma patients who received HSD, and will provide a basis for future in vitro and in vivo studies.

METHODS

Blood samples were obtained from 13 patients who were treated with 250 ml of HSD (Pharmacia AB, Uppsala Sweden) as a part of a larger prospective, randomized, double-blinded, placebo-controlled study evaluating the efficacy of the solution (1,2). This study was approved by the Human Subjects Review Committee at the University of California at Davis. The patients enrolled in the present study were randomly selected from the larger test population.

The patients were transported to the hospital by a Life Flight helicopter system, and all had significant hypotension upon entry into the study (systolic blood pressure <90). The HSD solution was administered intravenously, usually via percutaneously inserted catheters, over a period of 2-5 min en route to the hospital. All other aspects of the patients' care were those normally used. Additional fluid (Lactated Ringer's) was administered as clinically indicated. The time of administration of the HSD was noted and all additional fluid volumes given were recorded.

Upon arrival in the emergency room, a venous blood sample was taken for the measurement of hematocrit and plasma total protein, glucose, total carbohydrate, sodium and potassium levels. Dextran concentration was calculated as the difference between plasma total carbohydrate and glucose concentration (9).

In the text mean values and SEM values are given.

RESULTS

The mean weight of the patients was 72.3 ± 3.9 kg (Table I). The patients received 1108 ± 1399 ml of fluid prior to the administration of HSD. As each patient received 250 ml of HSD, the delivered dose was 3.6 ± 0.2 ml/kg. The time from the initiation of the dose of HSD to the collection of the blood sample was 26.7 ± 4.5 min. Over this period of time the patients received 845 ± 279 ml of additional fluids. Only one of the 13 patients died.

Upon arrival in the emergency room, the patients were significantly hemodiluted as indicated by low hematocrit ($27.4 \pm 2.8\%$) and total plasma protein levels (3.3 ± 0.4 g/dl) compared to normals (34-50% and 6.0-8.0 g/dl respectively) (Table II). Plasma concentration of sodium was increased (155 ± 1 mEq/l) compared to normal values, 135-145 mEq/l. One patient was clinically hypernatremic with plasma sodium levels greater than 160 mEq/l. Plasma potassium levels (4.0 ± 0.1 mEq/l) tended to be normal (3.5-5.0 mEq/l), with two patients being hypokalemic with concentrations less than 3.5 mEq/l. Plasma dextran concentrations ranged from 114.8 to 457.9 mg/dl with a mean of 243.9 ± 26.9 mg/dl.

DISCUSSION and CONCLUSIONS

The observed hemodilution upon admission to the emergency room reflects not only the infusion of crystalloid fluids, but also the transcapillary influx of fluid into the vascular space following hemorrhage and facilitation of this process by HSD administration (1-3,10,11). These processes result in a decrease in hematocrit and total plasma protein levels by simple dilution.

It has been suggested that hypernatremia and hypokalemia are of major concern in the administration of the HSD resuscitation solution (1,4,5). While clinical hypernatremia was observed in one of our patients, this has been reported to resolve within a short period of time (2). Hypokalemia was noted in two, 15%, of the patients. In one of the patients the incidence was borderline low with a potassium level of 3.4 mEq/l. In the other patient the potassium concentration was 2.9 mEq/l, and did not reflect a

significant hemodilution. No adverse effects associated with hypernatremia or hypokalemia were observed.

The circulating level of dextran, 244 mg/dl, was significantly less than expected. In a 70 Kg euvoletic man the plasma volume is assumed to be on the order of 2250 ml. If 250 ml of HSD which has 6% dextran (15 g) were added to this volume, the final dextran concentration would be 600 mg/dl. Due to the hemodilution effect of dextran, this concentration could actually achieve 500 mg/dl. As the trauma patients in the present study experienced significant hemorrhage, consequently reducing their plasma volume, the concentration of dextran should have been greater than 500 mg/dl. The low plasma levels observed in the present study suggest a rapid clearance sequestration or binding of dextran, a larger volume of distribution or hemodilution. The clearance of dextran has a half life on the order of six hours (9,12). As the blood samples were obtained within half an hour of HSD administration, the clearance of dextran would be minimal.

Fibrinogen is one of the plasma proteins cited to increase in response to tissue injury and other inducers of metabolic traumatic stress (13). Numerous studies have reported that dextrans may react with fibrinogen (7,14). If this conjugate is formed in vivo following HSD infusion, any dextran bound would be removed by TCA precipitation, rendering this dextran unavailable for assay. It is unknown whether such an effect could account, in part, for the lower than expected dextran concentrations observed in this study. Nevertheless, to avoid this possibility, we recommend performing dextran assays on serum samples. The dextran used in the present study had a mean molecular weight of 70k. Thus there was a quantity of lower molecular weight dextran which could have leaked out of the vascular space and been distributed into the interstitial fluid accounting for the increase in distribution volume. The decrease in dextran concentration could also be the product of hemodilution due to the large quantities of fluids administered following HSD. While hematocrit values agreed closely with the volume of fluid infused ($r=0.60$, $n=13$, $P<0.05$) a relationship to dextran levels was not present ($r=0.22$, $n=13$, $p=0.46$). Factors other than hemodilution due to the administration of additional fluids must further lower dextran levels. The lower

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levels of plasma dextran observed in trauma patients could be the product of a variety of factors and warrants further study to possibly improve the efficacy of HSD.

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Table I: Subject Characteristics

<u>Subject #</u>	<u>Body Wt (kg)</u>	<u>HSD Dose¹ (ml/kg)</u>	<u>Volume Infusion Prior to HSD (ml)</u>
1	70	3.6	0
2	80	3.1	0
3	60	4.2	0
4	70	3.6	400
5	85	2.9	2,300
6	100	2.5	100
7	55	4.6	200
8	58	4.3	1,200
9	80	3.1	3,800
10	80	3.1	4,000
11	72	3.5	1,000
12	50	5.0	500
13	<u>80</u>	<u>3.1</u>	<u>900</u>
x	72.3	3.6	1,108
SD	13.9	0.7	1,399
SEM	3.9	0.2	388

¹Each patient received 250 ml of HSD²This includes the 250 ml of HSD

<u>Subject #</u>	<u>Total Volume Infused² at Time of Sample (ml)</u>	<u>Time of Blood Sample Min Post HSD</u>	<u>Patient Outcome</u>
1	350	11	Lived
2	250	6	Lived
3	950	38	Lived
4	1270	25	Lived
5	2550	45	Lived
6	350	14	Lived
7	950	34	Lived
8	5270	63	Died
9	4250	20	Lived
10	5000	18	Lived
11	1800	10	Lived
12	950	28	Lived
13	<u>1450</u>	<u>35</u>	Lived
x	1,953	26.7	
SD	1,773	16.2	
SEM	492	4.5	

Table II: Blood Values

<u>Subj. #</u>	<u>Hematocrit (%)</u>	<u>Total Pro- tein (g/dl)</u>	<u>Sodium (mEq/l)</u>	<u>Potassium (mEq/l)</u>	<u>Glucose (mg/dl)</u>
1	40.9	6.2	150	3.4	22.4
2	32.5	4.4	159	3.9	155.9
3	32.0	3.0	157	2.9	183.6
4	21.8	3.2	154	4.2	350.5
5	17.3	1.9	157	4.5	199.7
6	38.5	5.2	151	3.7	0.8
7	34.9	3.2	151	3.6	101.9
8	7.7	1.1	157	4.1	193.6
9	28.6	3.7	152	4.1	29.5
10	27.6	3.4	154	4.3	74.6
11	12.2	1.6	154	4.5	221.6
12	29.4	4.2	165	4.6	85.0
13	<u>32.8</u>	<u>2.4</u>	<u>158</u>	<u>4.4</u>	<u>73.4</u>
x	27.4	3.3	155.3	4.0	130.2
SD	10.0	1.4	4.1	0.5	98.7
SEM	2.8	0.4	1.1	0.1	27.4

<u>Subject #</u>	<u>Total Carbohydrate (mg/dl)</u>	<u>Dextran (mg/dl)</u>
1	137.2	114.8
2	429.9	274.0
3	485.6	302.0
4	635.0	284.5
5	334.5	134.8
6	287.7	286.9
7	384.8	282.9
8	326.1	132.5
9	340.2	310.7
10	328.0	253.4
11	376.8	155.2
12	542.9	457.9
13	<u>254.3</u>	<u>180.9</u>
x	374.1	243.9
SD	128.2	96.8
SEM	35.6	26.9

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